NEUROTOXIN EXPOSURE TREATMENT RESEARCH PROGRAM

The U.S. Army Medical Research and Materiel Command is soliciting research proposals for studies on the pathophysiology, surrogate markers, mechanisms and treatment of Parkinson's disease and Parkinson's-related neurodegenerative conditions to include initiating causes, interaction of environmental and genetic risk factors, epigenetic modifying factors, with emphasis on exposure factors encountered in military operations which may be neurotoxic or lead to neurodegenerative conditions. An improved understanding of the pathophysiology of neurodegenerative diseases, emphasizing mechanisms underlying symptomology, generates advances in treatment interventions for Parkinson's disease and creates a basis for preventive measures against the risks of military operational hazards and military threat agents.

We solicit proposals on a wide range of basic and applied science, including but not limited to these specific areas of interest:

- **Determination of normal physiologic function of alpha-synuclein and alterations of alpha-synuclein function in the progression of Parkinson's disease.**
- **Determination of mechanisms of integration of proteasomal, mitochondrial, synaptic and nuclear function in normal dopaminergic function.**
- **Determination of non-motor symptoms associated with PD and development of criteria for standardized diagnosis.**
- **Development of sensitive, cost-effective biomarker(s) for diagnosing PD (including during the pre-symptomatic phase) and evaluating progression.**
- **Quantification of dose/type relationship of exercise(s) and neuroprotective effect**
- **Determination of environmental influences modulating mitochondrial or other cellular organelle function and specific environmental influences resulting in long-lasting or permanent dopaminergic dysfunction in PD.**
- **Clarification of neuronal/ glial interaction in Parkinson's disease, in relation to: (a) disease initiation and progression; (b) the inflammatory response on both cell types; (c) environmental and occupational exposures that affect intracellular organelle structure and function (e.g. protein trafficking, mitochondrial structure and energy production); (d) brain regional differences with respect to relative susceptibilities, and thresholds of impact that increase probability of development of Parkinsonism, as they relate to glia-mediated inflammatory responses.**
- **Development of methodology to test the Braak hypothesis of anatomical progression of PD and development of disease models specific for the various hypothesized initiating causes of PD**
- **Presynaptic/post synaptic model development of normal and abnormal dopaminergic function.**
- **Determination of mechanisms of epigenetic modification that are responsive to environmental exposures and result in prolonged or permanent alteration of neurotransmitter function.**
- **Clarification of mechanisms of tremor development in Parkinson's disease and identification and validation of specific therapeutic strategies based on identified mechanisms.**
- **Development or improvement of non-dopaminergic therapies for PD. (This could include exercise, DBS, TMS, non-dopaminergic drugs, targets other than basal ganglia**

Proposals will be selected from those submitted in response to this announcement and proposals that address the stated topics that were submitted in response to the USAMRMC BAA 05-1. Selections will be based on scientific quality/merit, assessed under peer review and military relevance. Projects are typically 2-4 years in duration and must be completed by 30 Sep 2011. Program projects will not be considered. No proposals will be funded that are dependent upon completion of an interagency agreement. Preference will be given to "concept exploration" proposals (CEP) that allow investigators to conduct pilot studies and develop preliminary data for novel hypotheses that fall within the specific topic areas, with the intent that full proposals submitted to future solicitations may further expand on CEP successes; CEP duration should not exceed 24 months; costs for these studies should not exceed $250K per year, inclusive of direct and indirect costs; approximately 10 concept exploration proposals are expected to be funded in addition to approximately 5 proposals having significant pilot and literature support. Previously untested concepts will receive priority. Proposals selected for award are not considered renewable. Proposals must be submitted according to general instructions contained in the Broad Agency Announcement 05-1 (BAA 05-1) (see http://www.usamraa.army.mil). Letters of intent containing a proposed title, brief description of project scope (<150 words), and investigator and institution identification, are encouraged and should be sent by 14 April 2006 to: Commander, U.S. Army Medical Research and Materiel Command, ATTN: MCMR-AAA (Neurotox), 820 Chandler Street, Fort Detrick, MD 21702-5014.

Letters of intent are for planning purposes and investigators will NOT be sent any response to the letters of intent. Full proposals are due not later than 2:00 pm EST, Monday, 15 May 2006. Proposals must be submitted according to procedures provided at the United States Army Medical Research Acquisition Activity web site (see http://www.usamraa.army.mil and in accordance with the Broad Agency Announcement 05-1 (BAA 05-1).